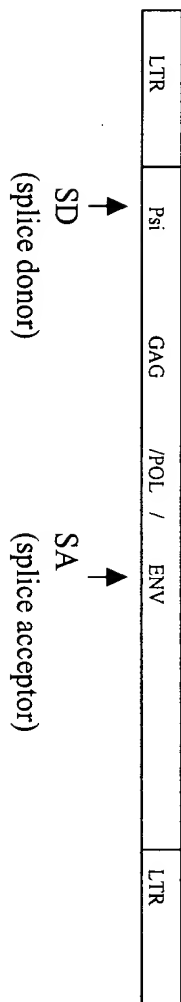
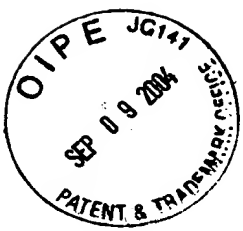
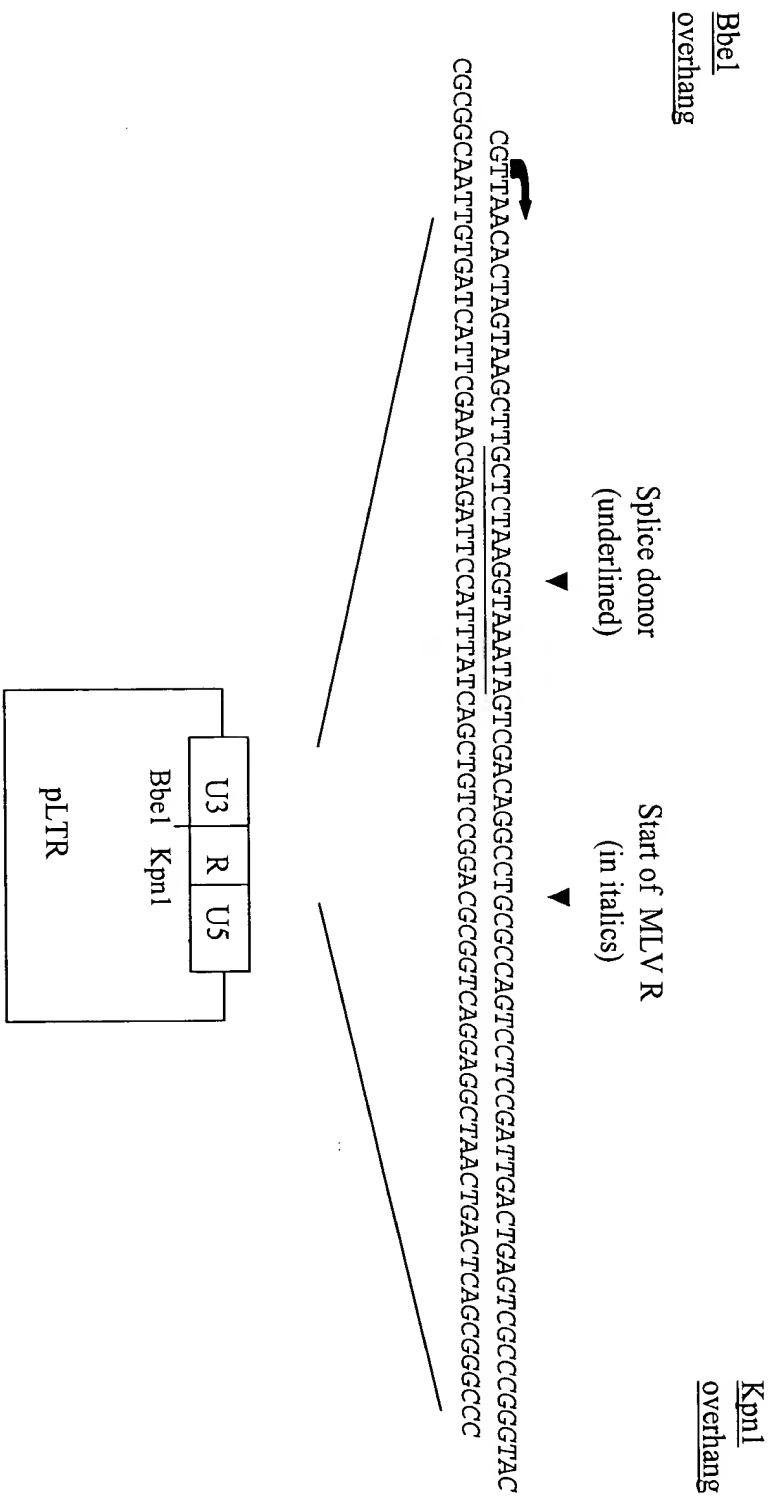


Figure 1



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Figure 2



**Figure 3**

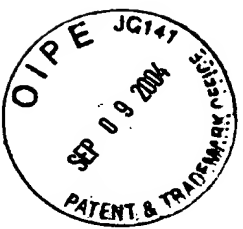
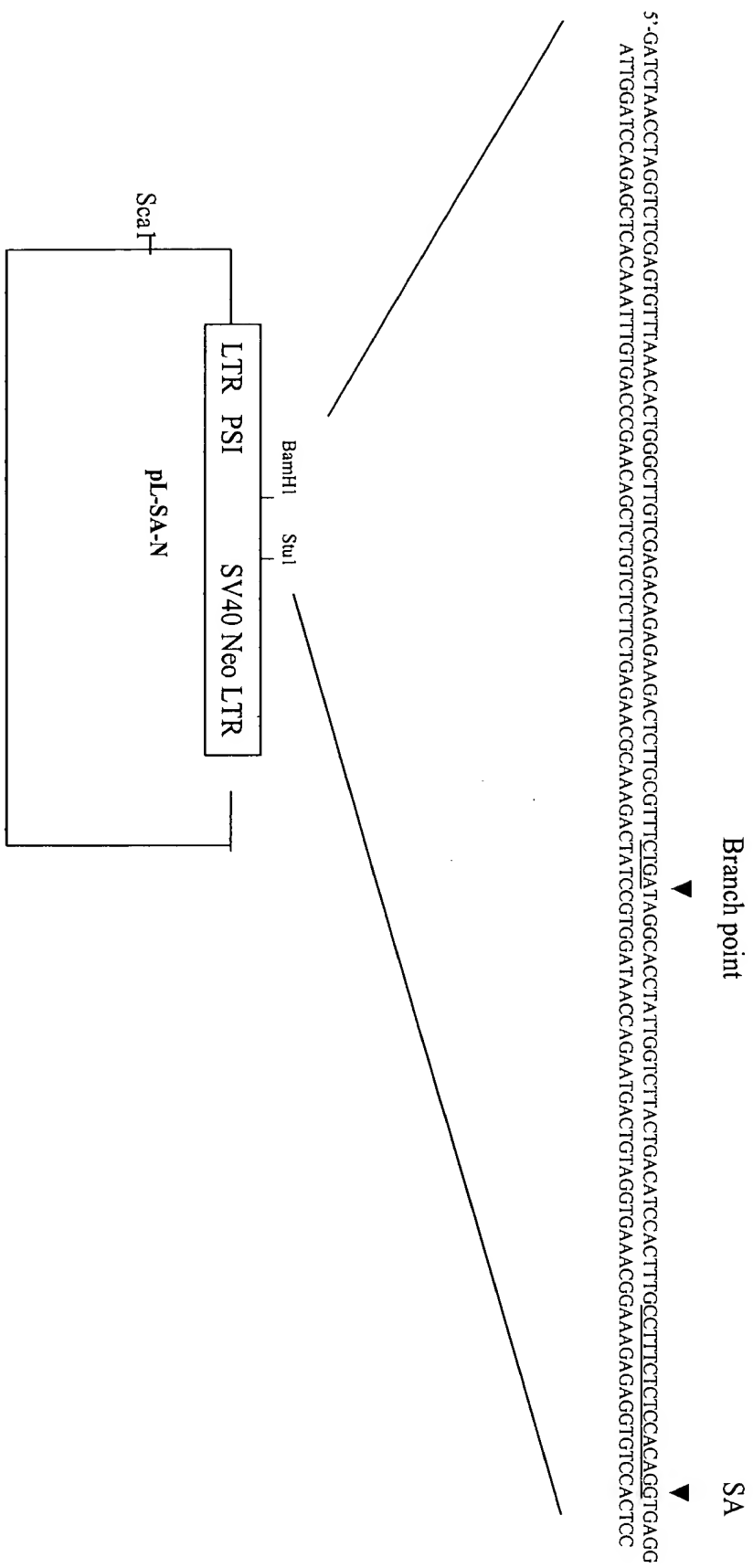
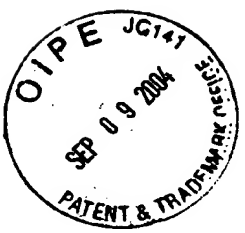
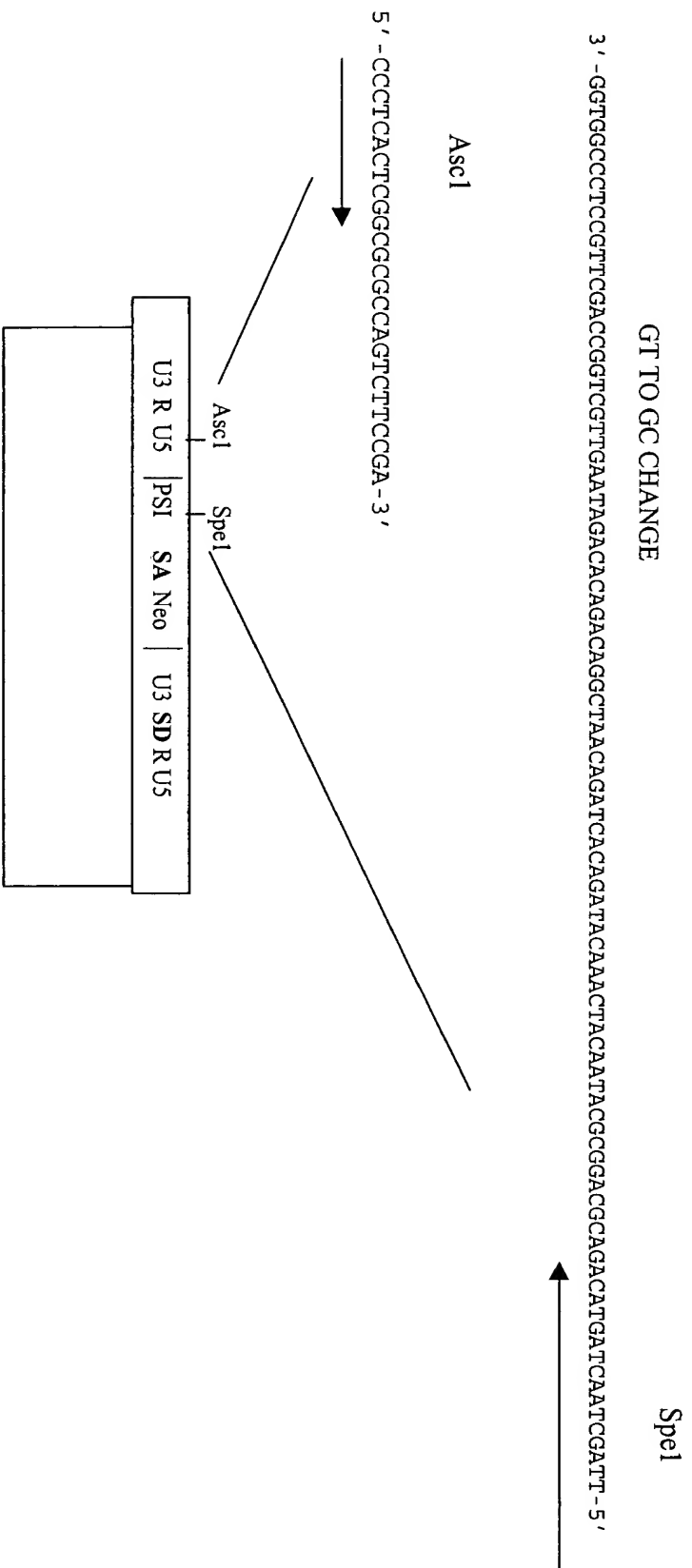


Figure 4



## Figure 5

Figure 6

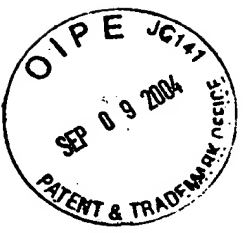
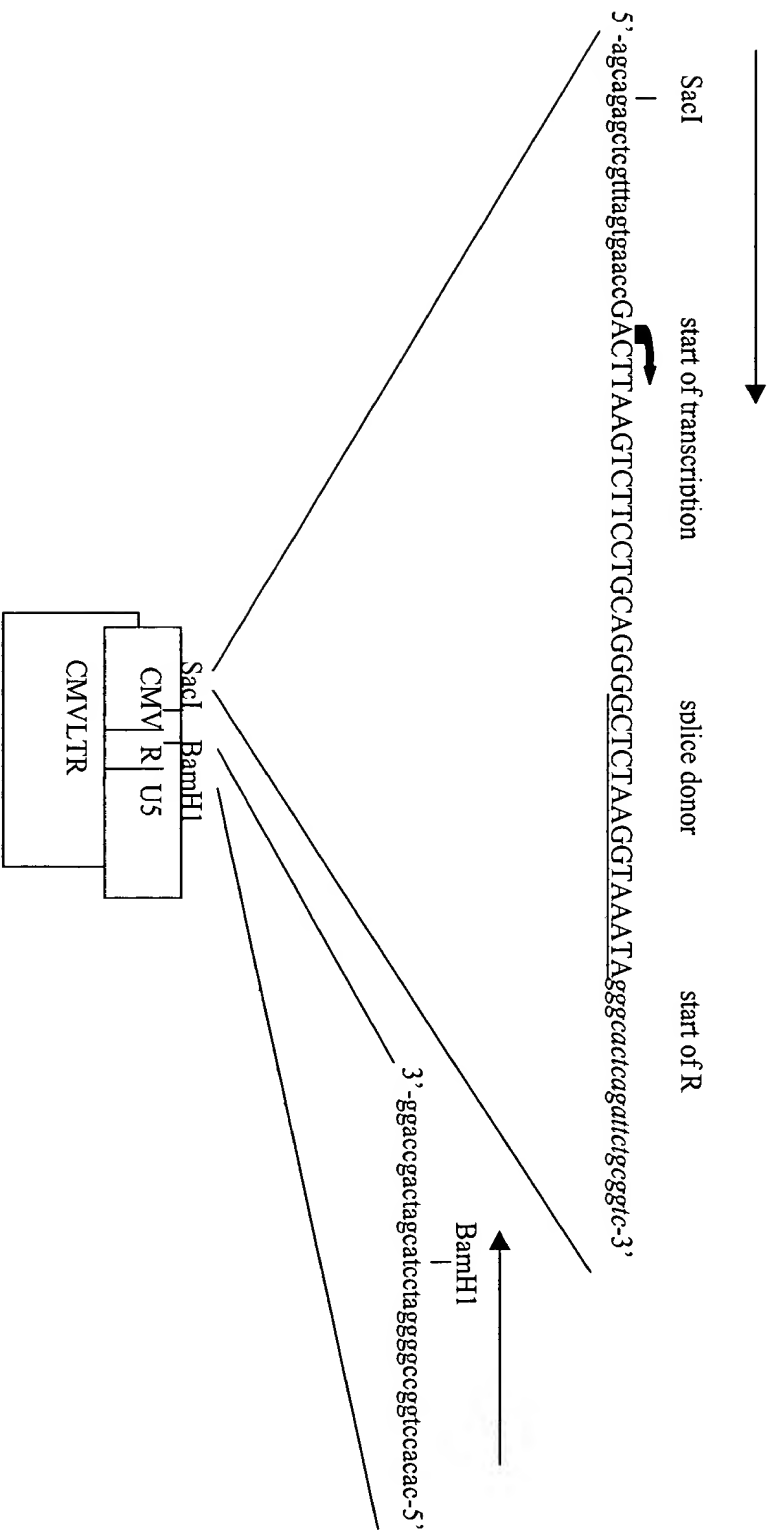
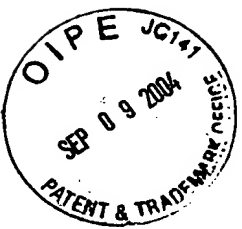
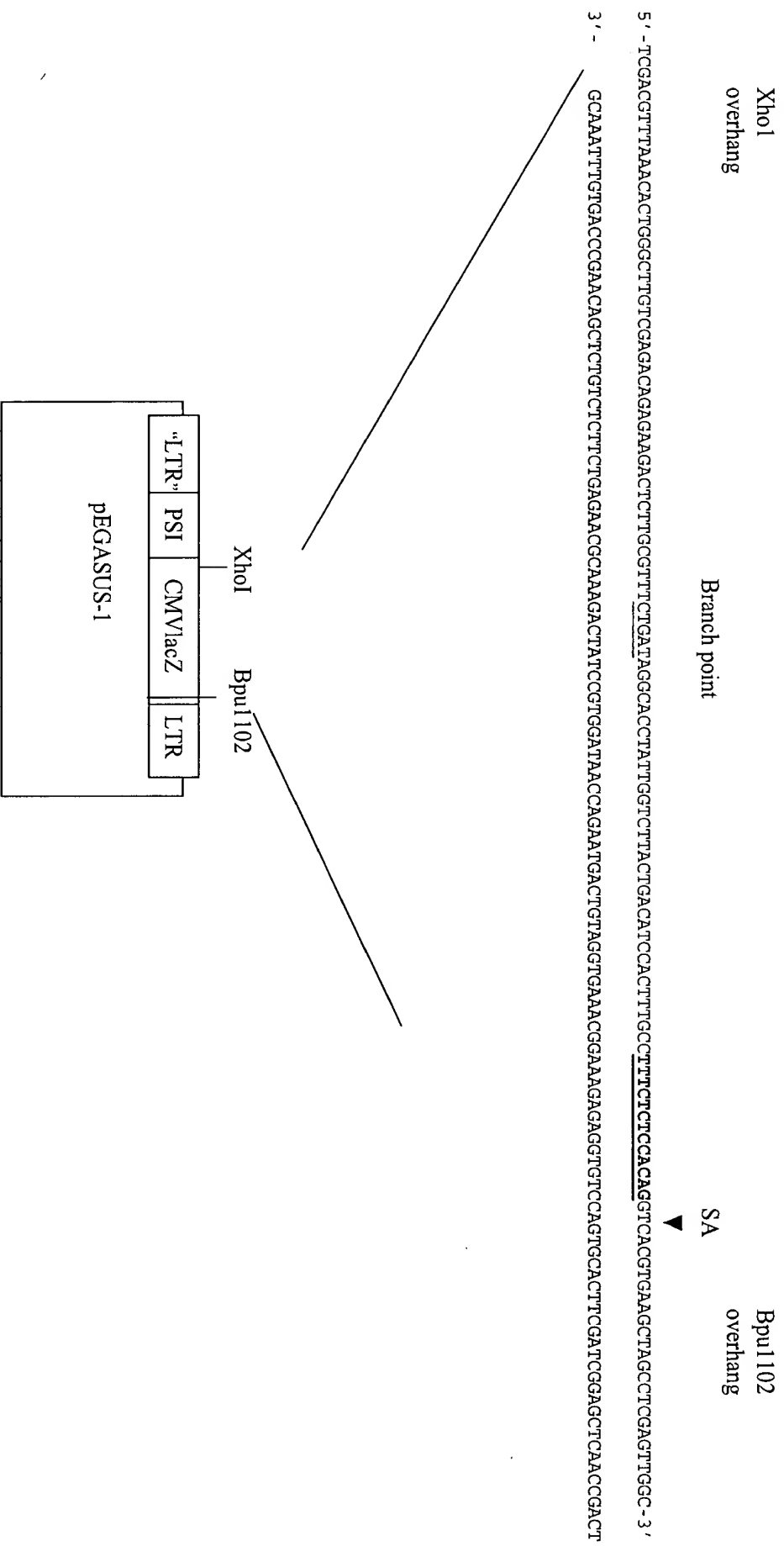
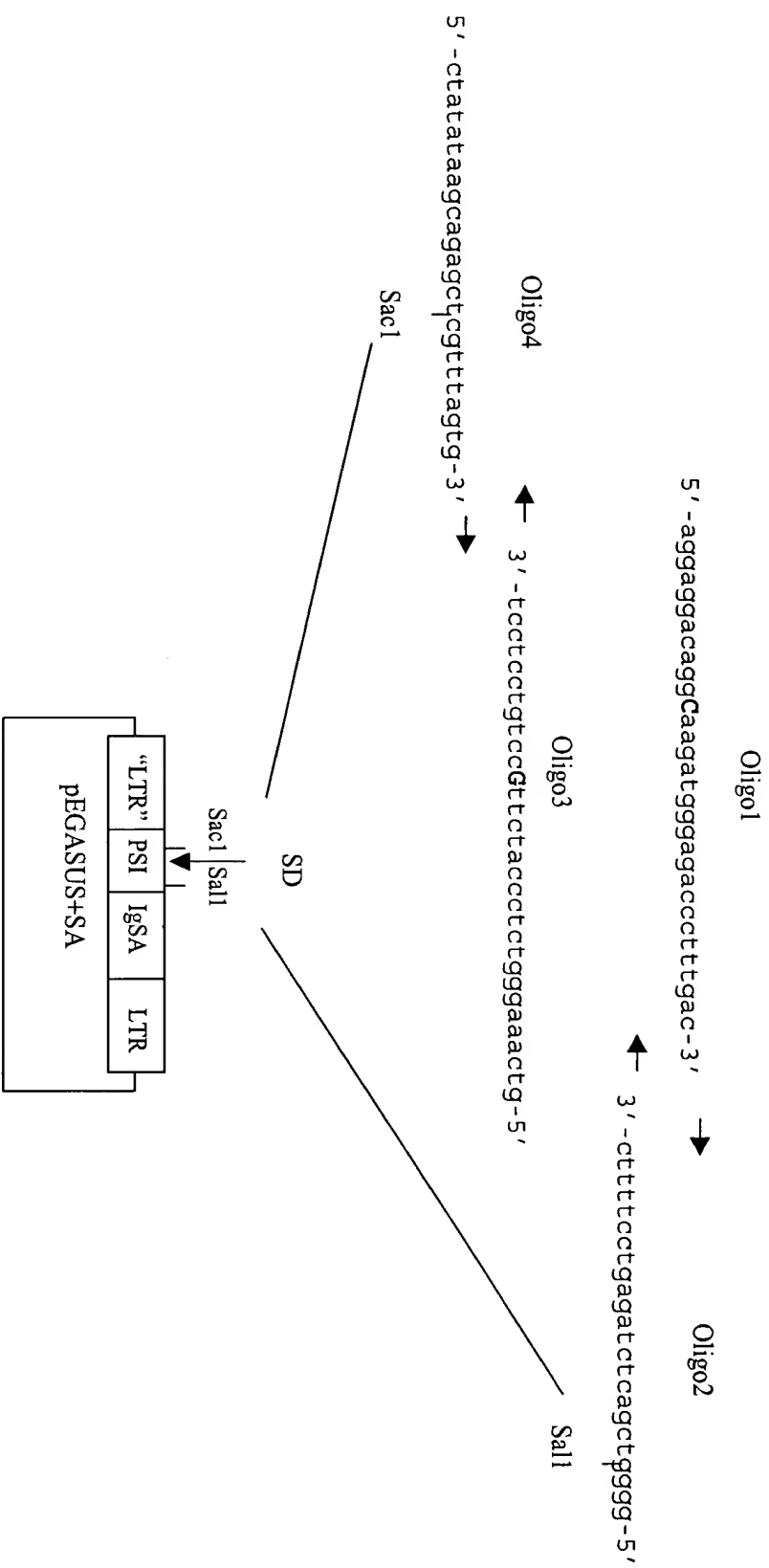


Figure 7



**Figure 8**





**Figure 9**

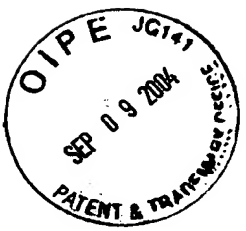
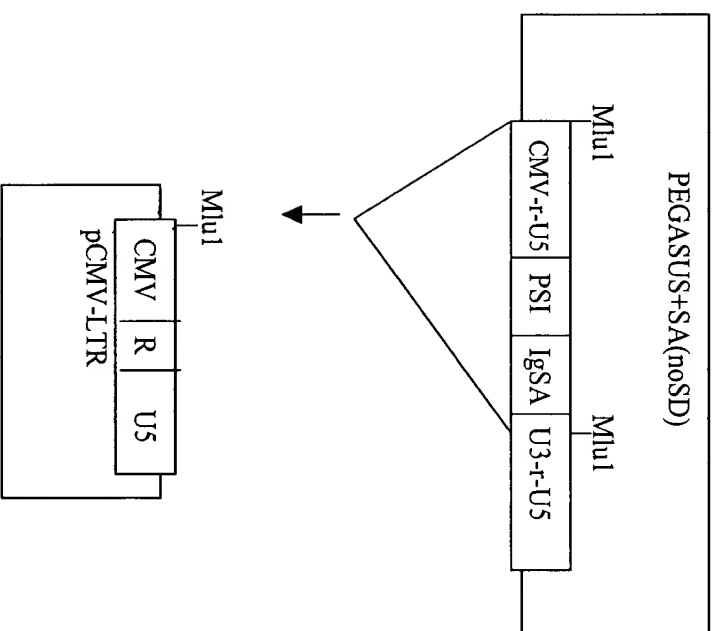
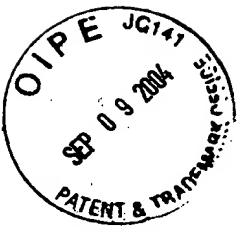
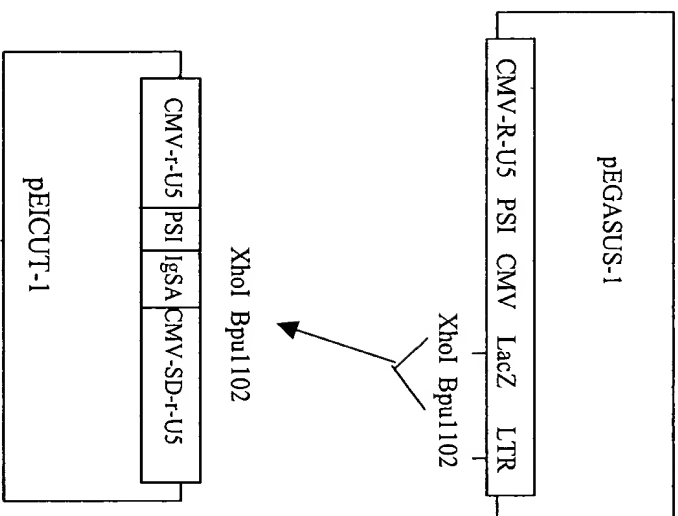


Figure 10



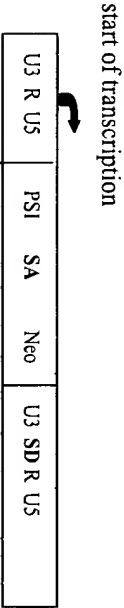
[illegible]

### Figure 11B



Figure 12

(A) pICUT vector in transfected cells



(B) pICUT vector in transduced cells

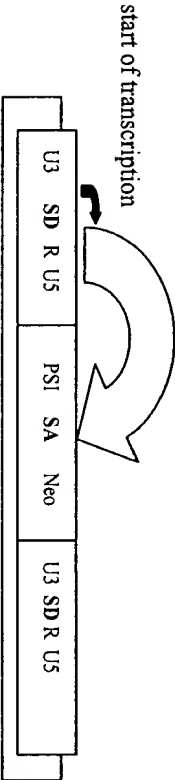
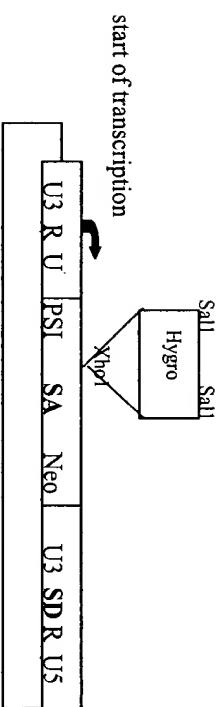


Figure 13

(A) Vector configuration in transfected cells



(B) Vector configuration in transduced cells

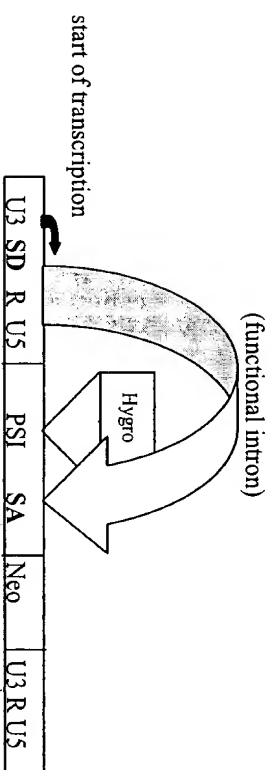
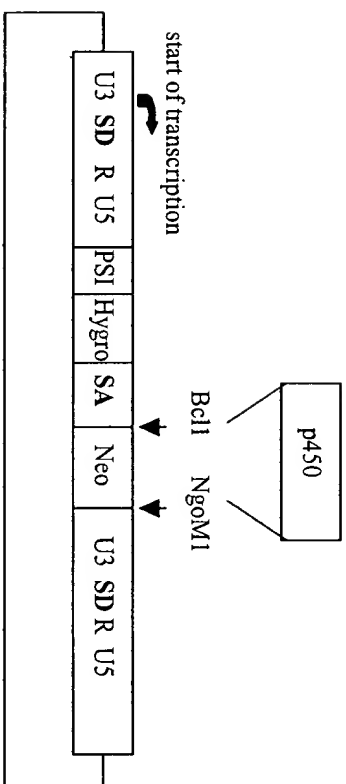
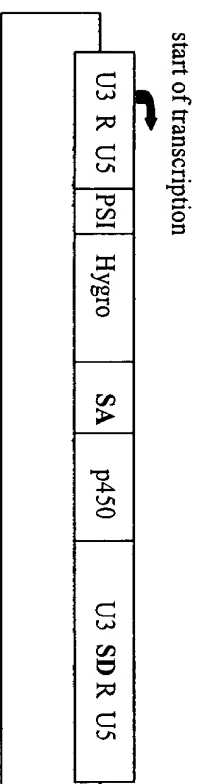


Figure 14

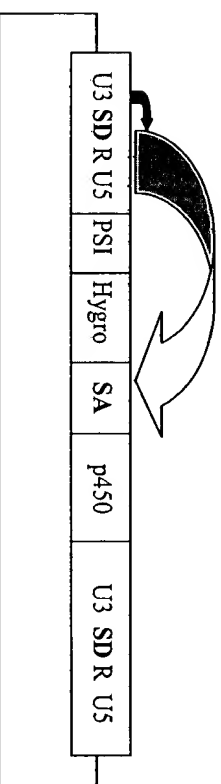
(A) p450 insertion



(B) Hygromycin expression in transfected cell



(C) p450 expression in transduced cell



**Figure 15**

3'end of pol	5'-ATG CGT TCA ACG CTC TCA AAA CCC CTT AAA AAT AAG
5'altered 4070A	5'-ATG GCC AGA AGC ACC CTG AGC AAG CCA CCC CAG GAC
	GTT AAC CCG CGA GGC CCC CTA ATC CCC-3'
	AAA AAT CCC TGG AAA CCT CTG ATC GTC-3'





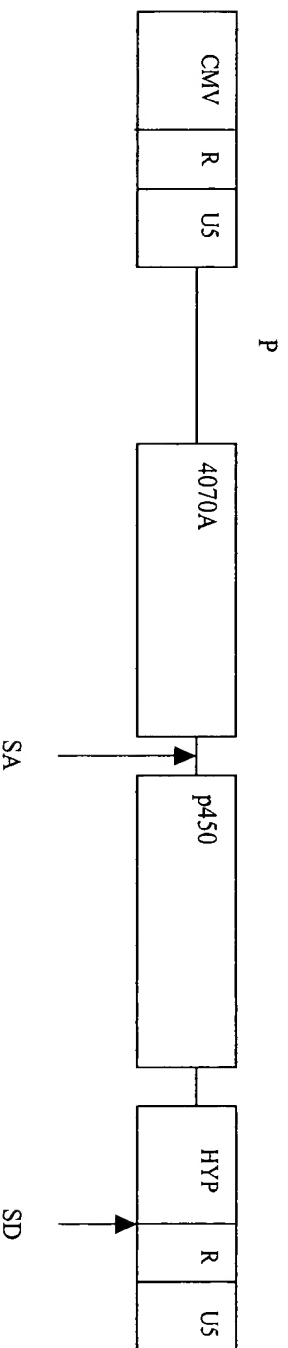
Figure 16

ATGGCCAGAA GCACCTGTAG CAAGCCACCC CAGACAAAA TCAATCCCTG GAAACCTCTG  
ATCGTCAATGG GAGTCCTGTT AGAGTAGGG ATGCAGAGA GCCCCATTC AGGTC  
TTTAATGTAA CCTGGAGAGT CACCAACCTG  
ATGACTGGGC GTACCGCCAA TGCCACCTCC CTCCTGGGAA CTGTACAAGA TGCCTTCCCA  
AAATTATATT TTGATCTATG TGATCTGTGC GGAGAGAGT GGGACCTTC AGACCAGGAA  
CCGTATGTGC GGTATGGCTG CAAGTACCCC GCAGGGAGAC AGCGACCCG GACTTTGAC  
TTTTACGTGT GCCCTGGGCA TACCGTAAAG TCGGGGTGTG GGGACCCAGG AGAGGGCTAC  
TGTGTAAAT GGGGTGTGA AACCACCGA CAGGCTTACT GGAAGCCAC ATCATCGTG  
GACCTAATCT CCTTAAGCG CGGTACACC CCTGGGACA CGGATGCTC TAAAGTTGCC  
TGTGGCCCTT GCTACGACCT CTCCAAGTA TCCAATTCTT TCCAAGGGG TACTCGAGG  
GGCAGATGCA ACCCTTAGT CTAGAATTG ACTGATGCAG GAAAAAGG TAACTGGAC  
GGGCCCAAT CGTGGGACT GAGACTGTAC CGACAGGAA CAGATCTTAT TACCATGTTT  
TCCCTGACCC GGCAGGTCTT TAATGTGGA CCCCAGTCC CCATAGGGCC CAACCCAGTA  
TTACCCGACC AAAGACTCCC TTCTCACC AATAGATTG TACCGGCTCC ACAGCCACT  
AGCCCCCTCA ATACAGTTA CCCCCCTCC ACTACAGTA CACCTCAAC CTCCCCTACA  
AGTCCAAGTG TCCACAGCC ACCCCAGGA ACTGGAGATA GACTACTAGC TCTAGTCAA  
GGAGCCTATC AGCGCTTAA CCTCACCAT CCCGACAAGA CCCAAGATG TTGGCTGTGC  
TTAGTGTGG GACTTCCTTA TTACGAAGGA GTAGCGGTG TGGCACTTA TACCAATCAT  
TCCACCGCTC CGGCCAATG TAGGCCACT TCCACATA AGCTTACCCT ATCTGAATG  
ACAGAGAGG GCTATGCAT GGGGACAGTA CCTAAATC ACCAGGCTT ATGTAACAC  
ACCCAAGCG CCGCTCAG ATCCTACTAC CTTGACGAC CCGCCGAC AATGTGGCT  
TGCAGCACTG GATTGACTCC CTGCTGTCC ACCACGCTG TCAATCTAAC CACAGATTAT  
TGTGTATTAG TTGAACCTG GCCCAGAGTA ATTTACCCT CCCCAGTTA TATGTATGCT  
CAGCTTGAA AGCGTACCAA ATATAAAGA GAGCAGTAT CATTGACCT GGCCCTTCTA  
CTAGGAGGAT TAACCATGG AGGATTTGA GCTGGAATAG GACGGGGAC CACTGCCCTA  
ATTAAAACC AGCAGTTGA GCAGTTCAT GCCGTATCC AGACAGCTT CAAGAGTTC  
GAAAAGTCAA TTACCAACCT AGAAAGTCA CTGACTCGT TGTCTGAAGT AGTCTACAG  
AACCGCAGAG GCTAGATTG GCTATTCCTA AAGGAGGAG GTCTCTGCG AGCCCTAAAA  
GAAGAATGTT GTTTTATGC AGACACACG GGGCTAGTGA GAGACAGCAT GGCCTAATTA  
AGAGAAAGGC TTAATCAGAG ACAAAAACTA TTGAGACAG GCCAAGGATG GTTCGAAGGG  
CTGTTAATA GATCCCCCTG GTTTACACC TTAATCTCA CCATCATGGG ACCTTAATA  
GTACTCTTAC TGATCTTACT CTTTGACCT TGCATTCTCA ATCATGCTT CCAATTGTT  
AAAGACAGGA TCTCATGCT CAGGCTCTG GTTTGACTC AGCAATATC CCAGCTAAAA  
CCCATAGAGT ACGAGCATG A

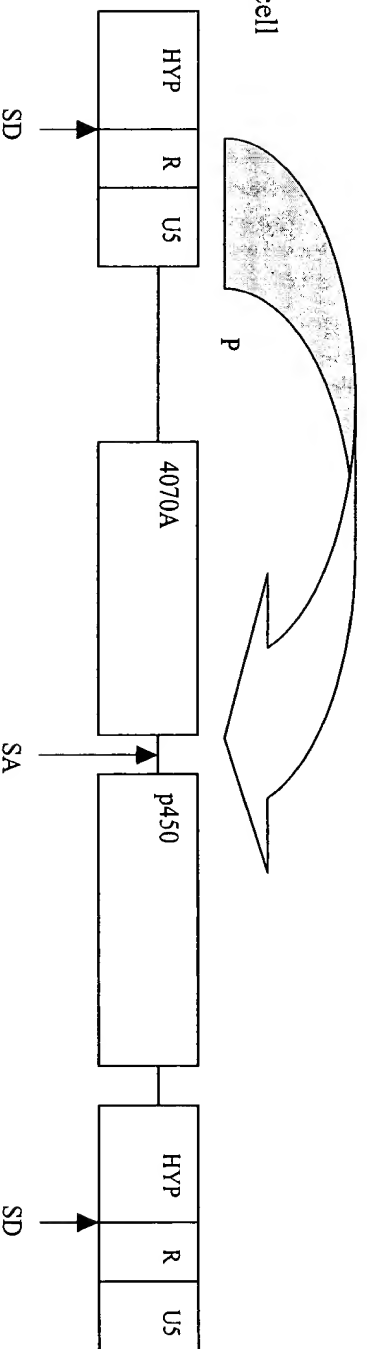


**Figure 17**

Packaging cell



Transduced cell



CMV=CMV Promoter

HYP= Hypoxia responsive promoter

P= MLV packaging signal

4070A= MLV amphotrophic Env gene

p450= p450 reductase encoding cDNA

SD= Splice donor

SA= Splice acceptor

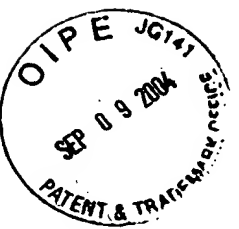


Figure 18

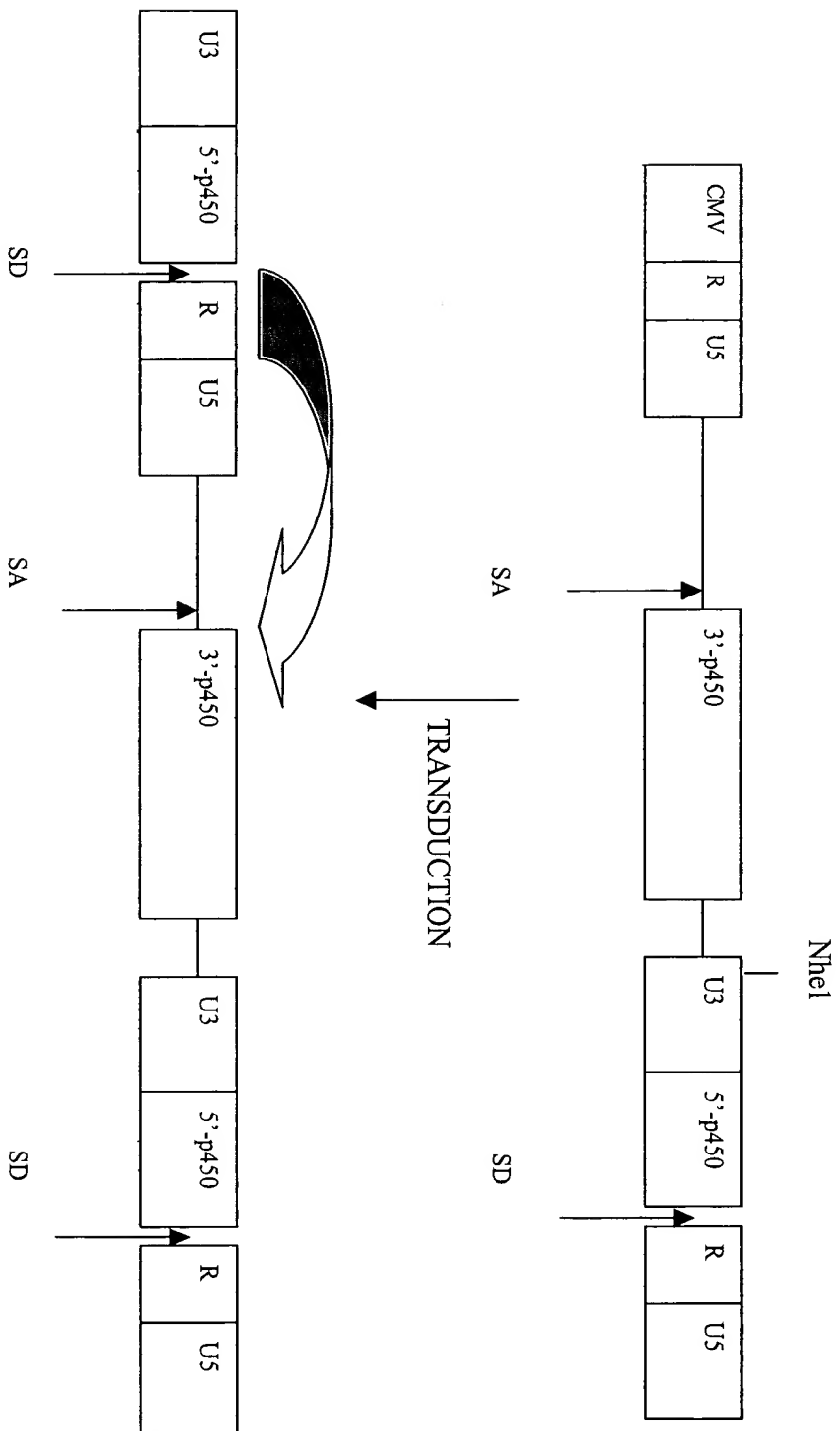
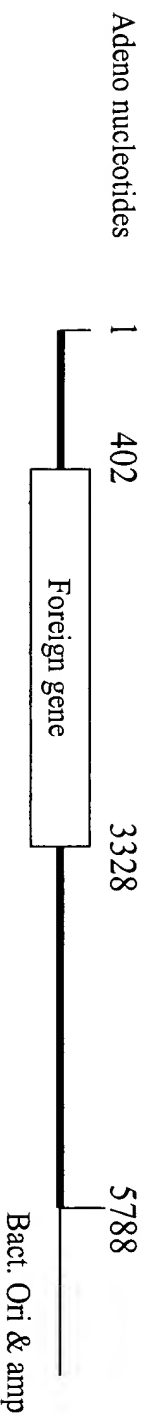
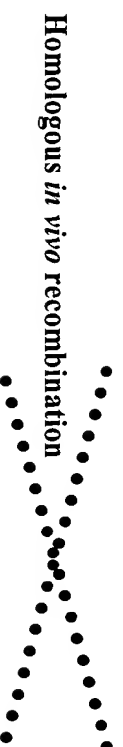


Figure 19

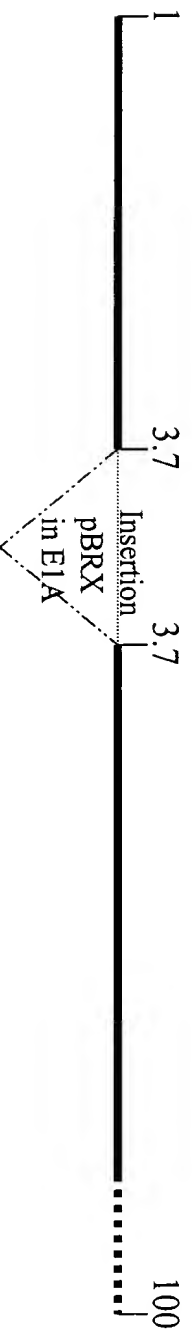
Transfer vector (shown linear)



pJM19 (shown linear)



Adeno Map units



40 kb plasmid - too large to be packaged into nucleocapsids



Packagable recombinant adenovirus

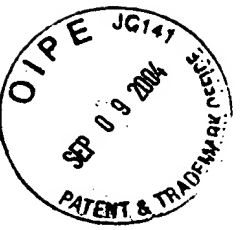
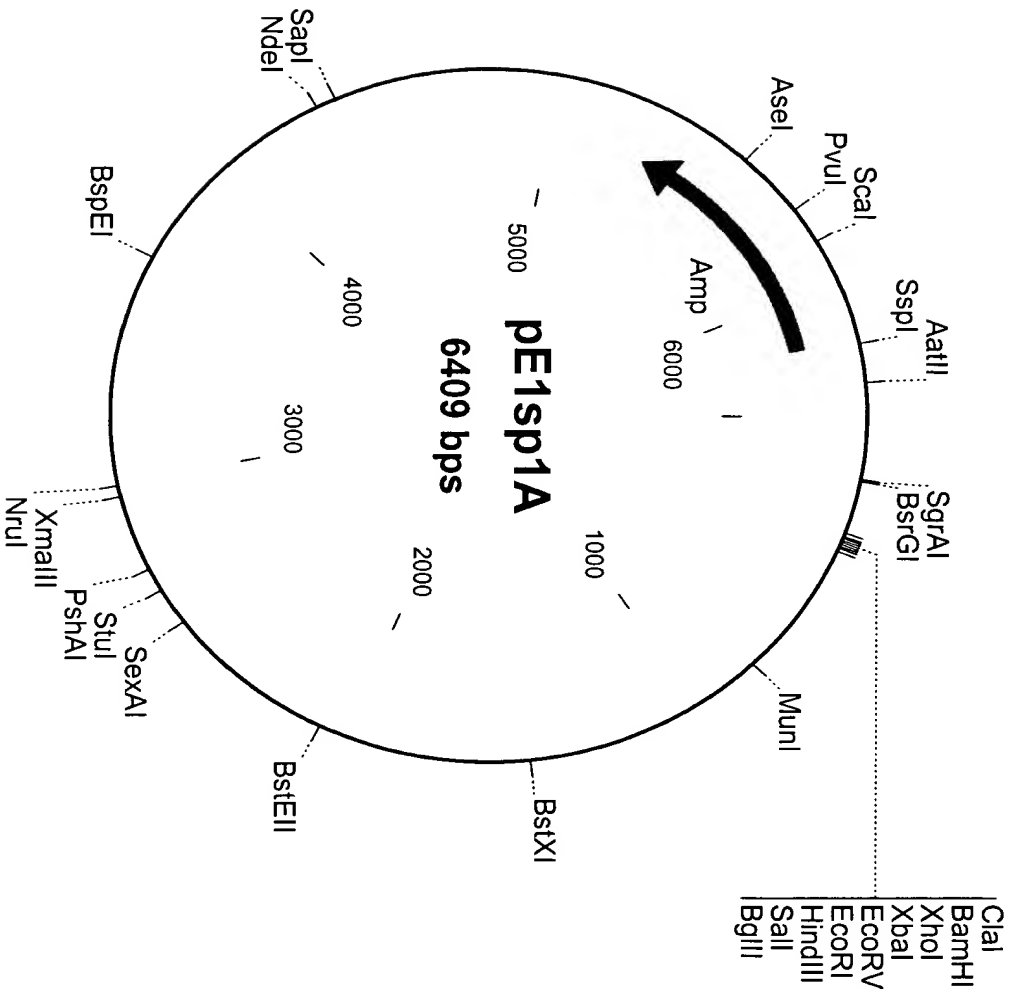


Figure 20



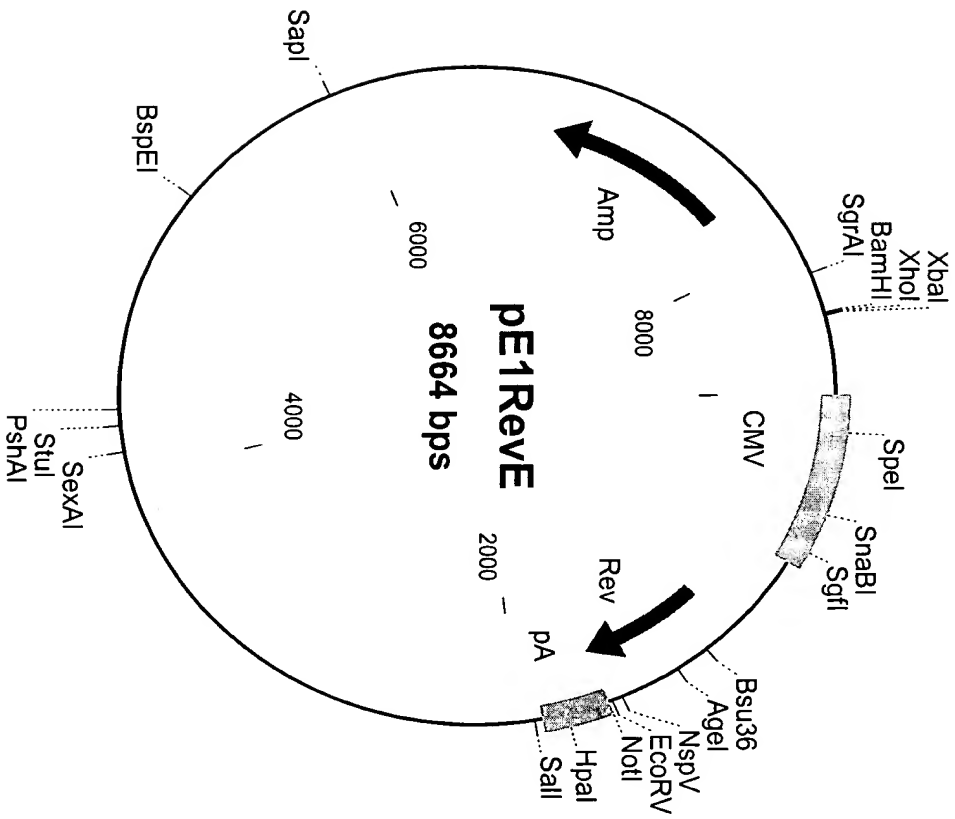
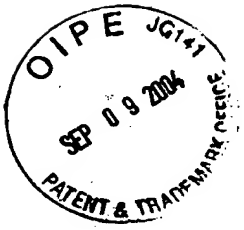


Figure 21

Figure 22

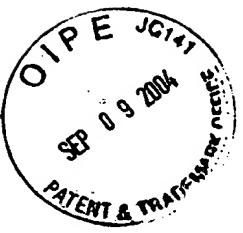
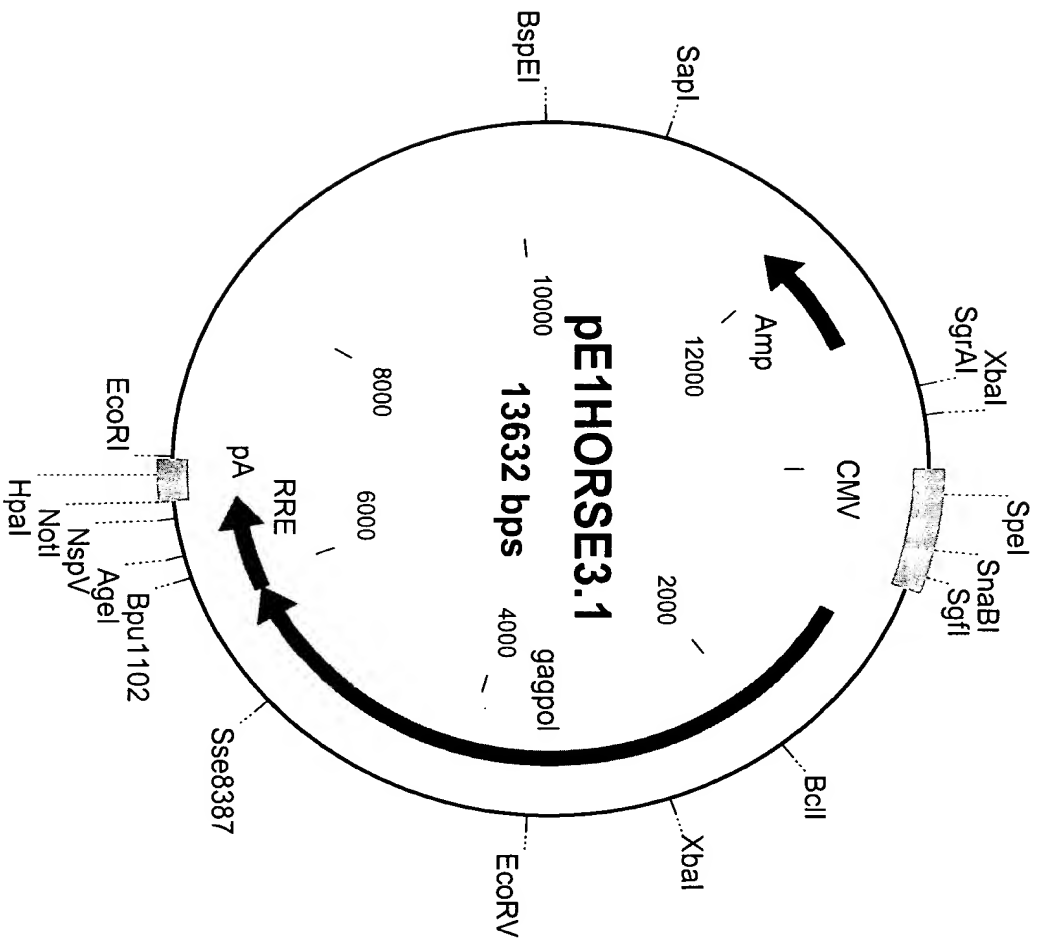


Figure 23

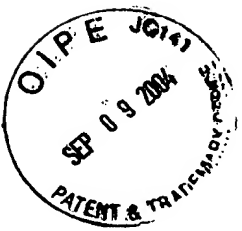
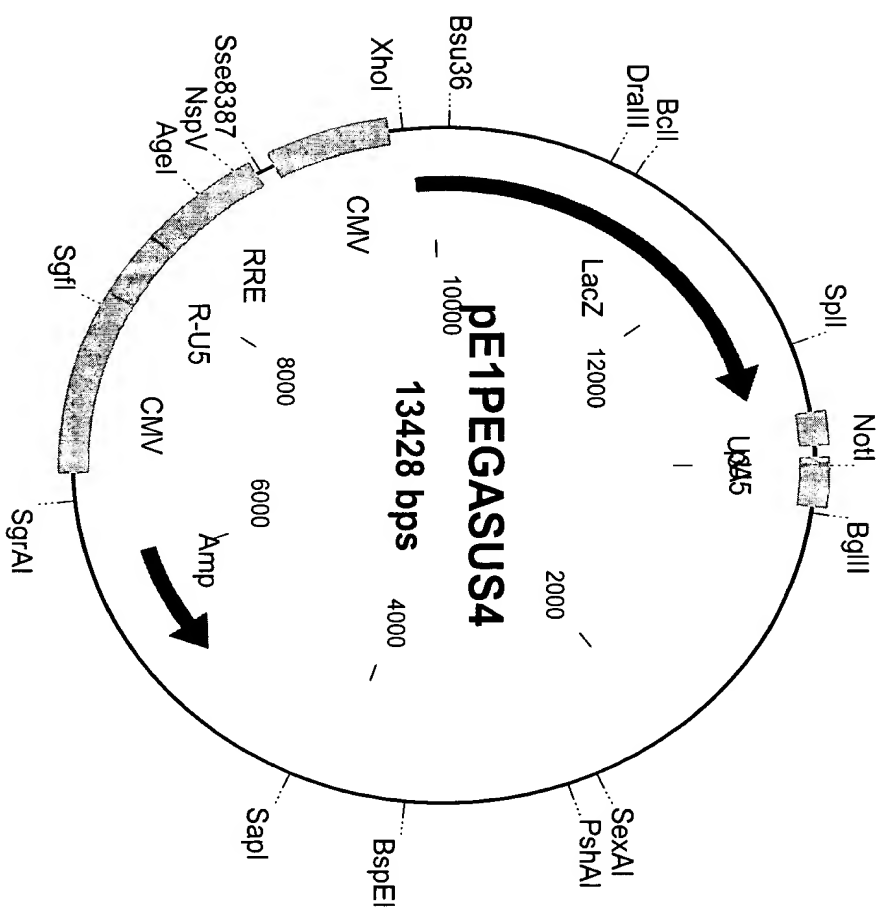




Figure 24

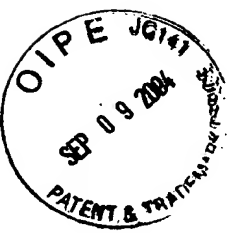
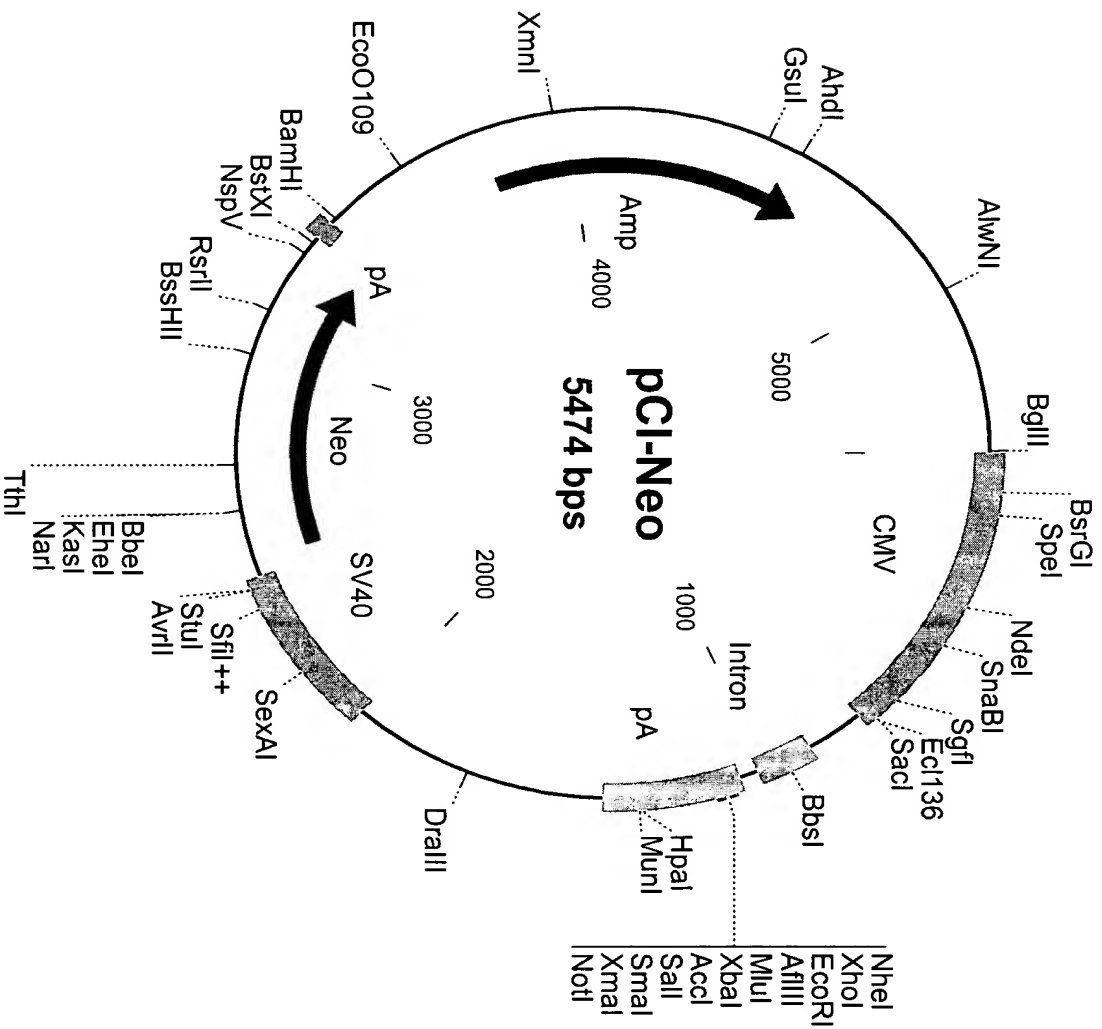
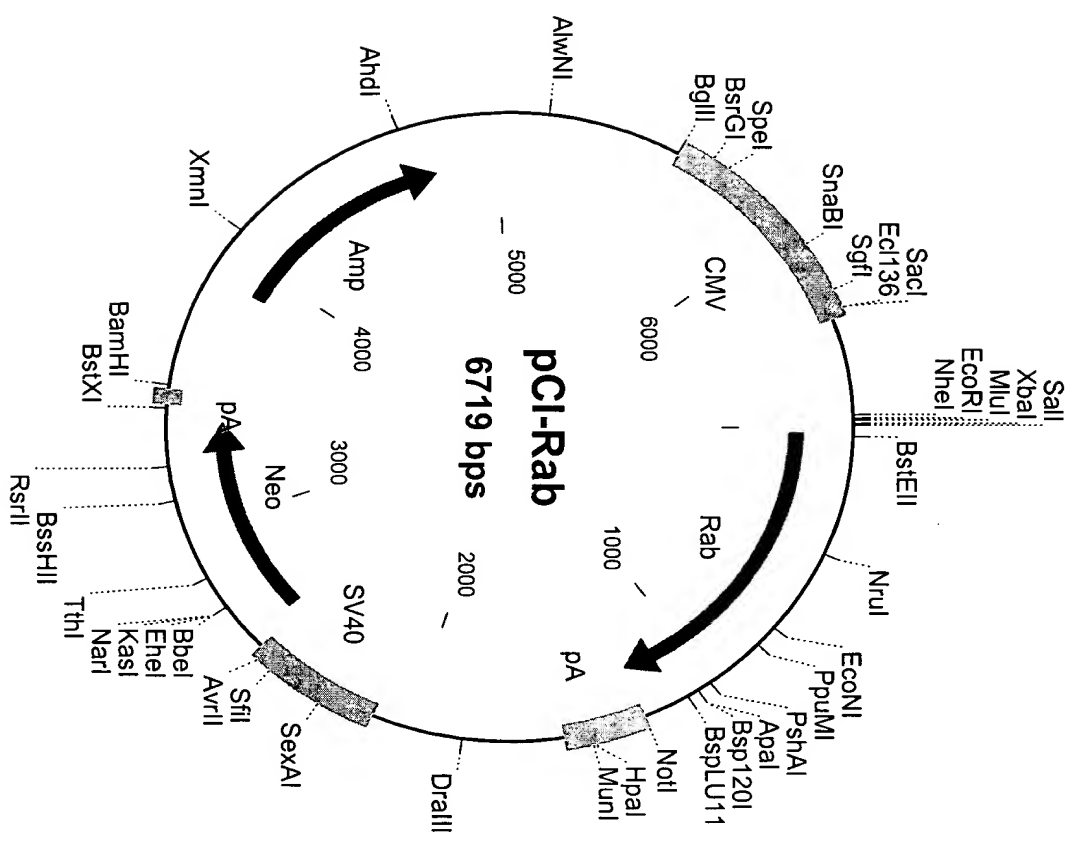
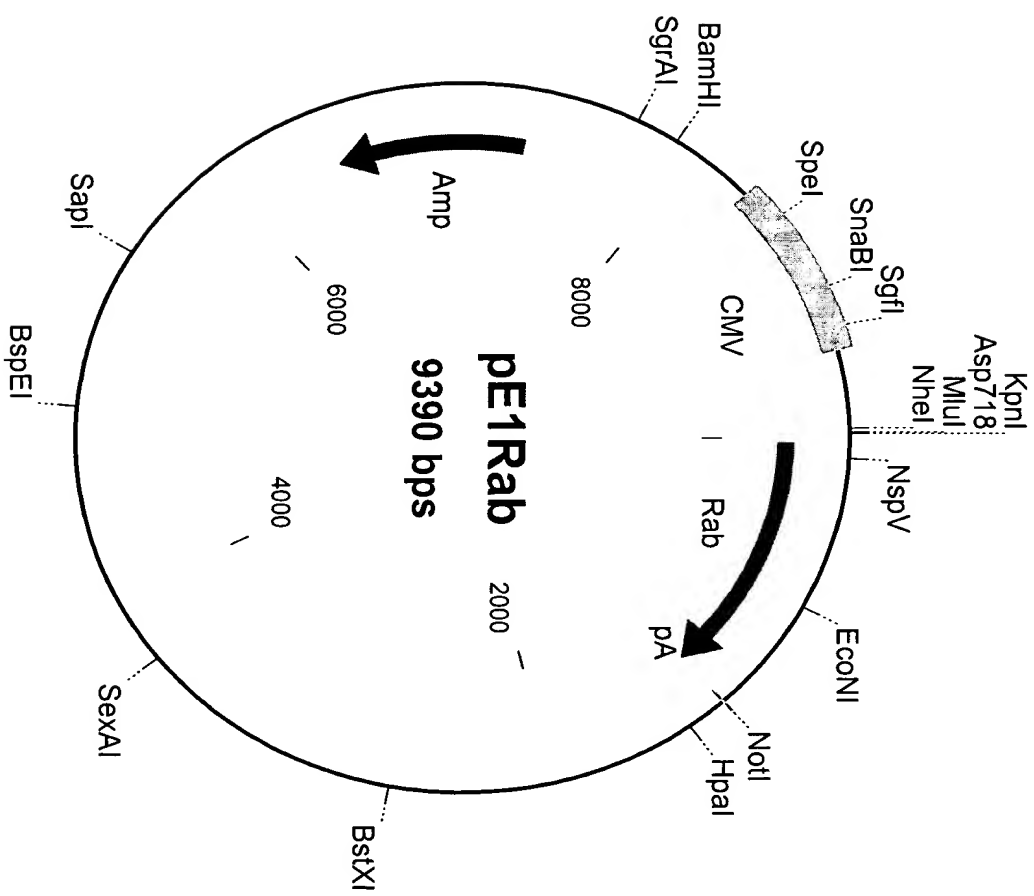


Figure 25

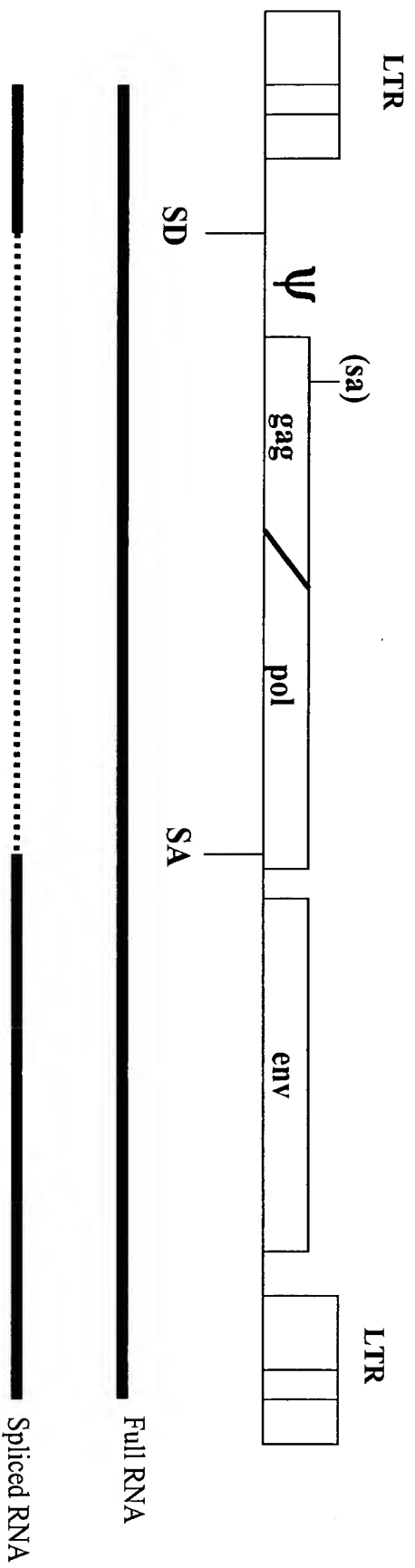


**Figure 26**



**Figure 27a**

**A) Natural splicing configuration**



SD = Splice donor

SA = Splice acceptor

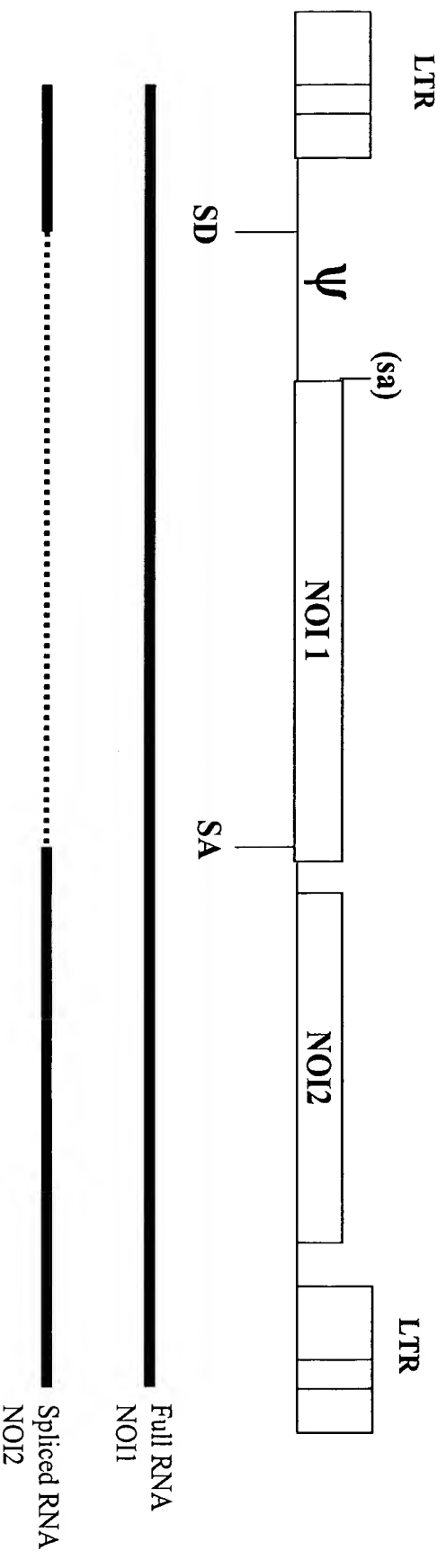
(sa) = cryptic splice acceptor

$\Psi$  = packaging site

**Figure 27b**

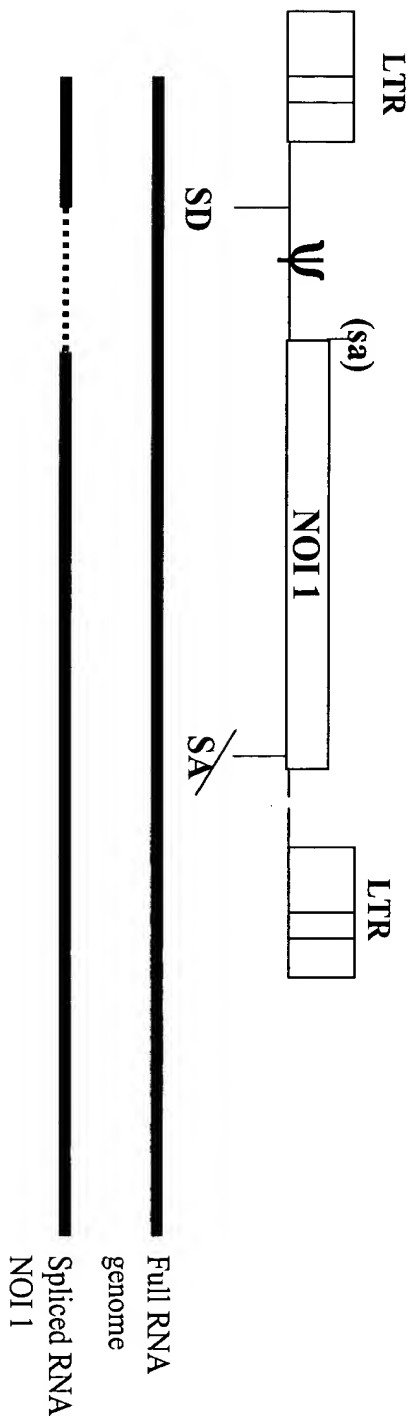
**Splicing configurations in known vectors**

e.g. LTRSVX



e.g. N2

Figure 27b cont.



e.g. MFG

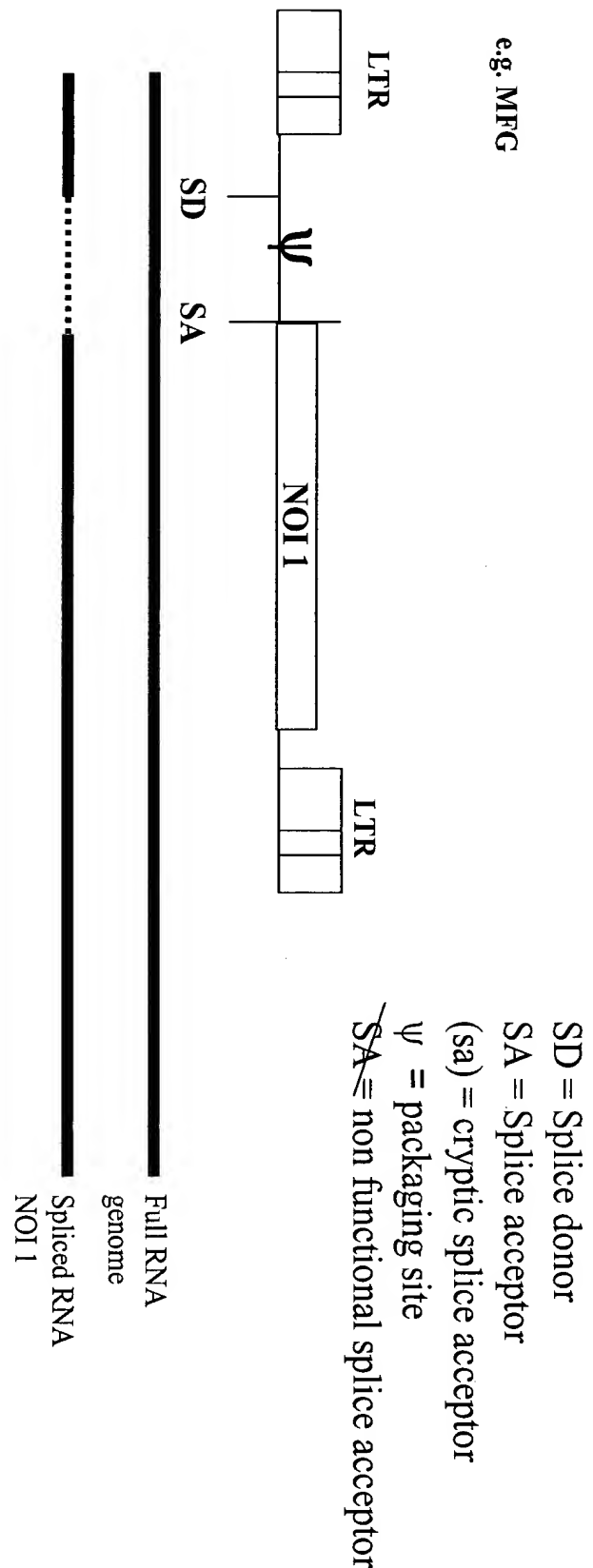
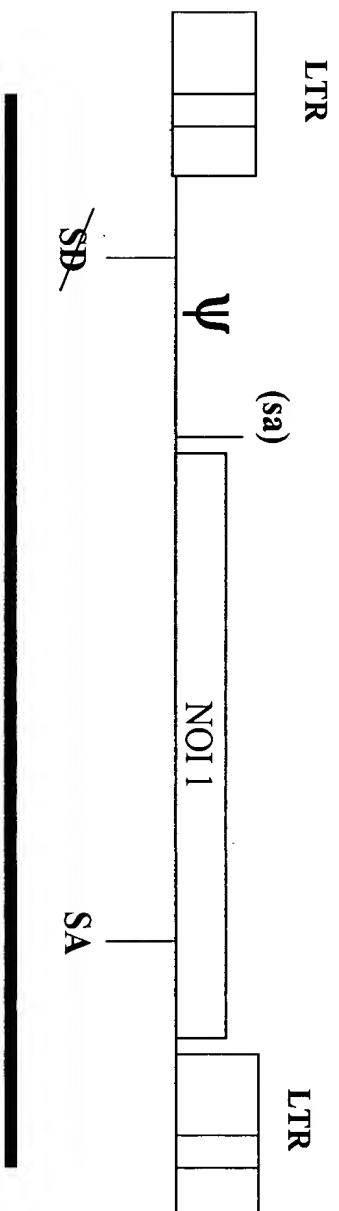


Figure 27b cont.

e.g pBABE

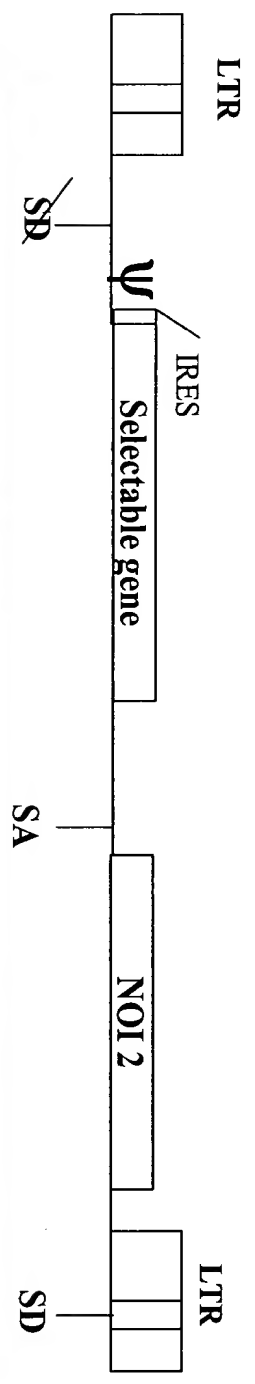


Full RNA  
genome and  
NOI 1

~~SD~~ = Non functional splice donor  
SA = Splice acceptor  
(sa) = cryptic splice acceptor  
ψ = packaging site

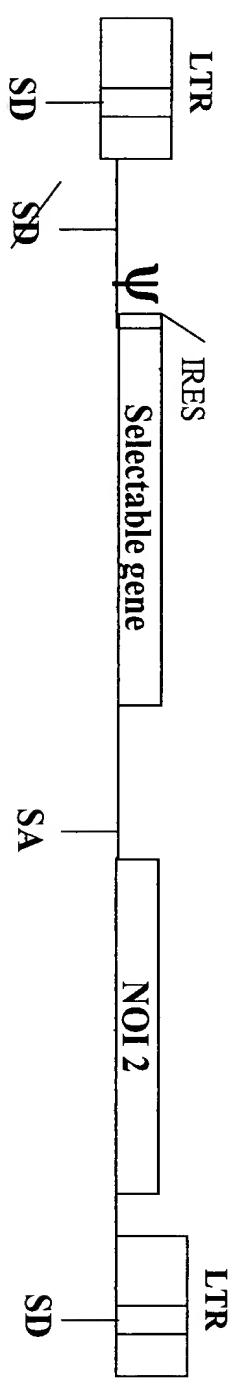
**Figure 27c**

**Pro-vector**



SD = Splice donor  
~~SD~~ = non functional splice donor  
 SA = Splice acceptor  
 (sa) = cryptic splice acceptor  
 $\psi$  = packaging site  
 IRES = internal ribosome entry site (optional)

**Vector**

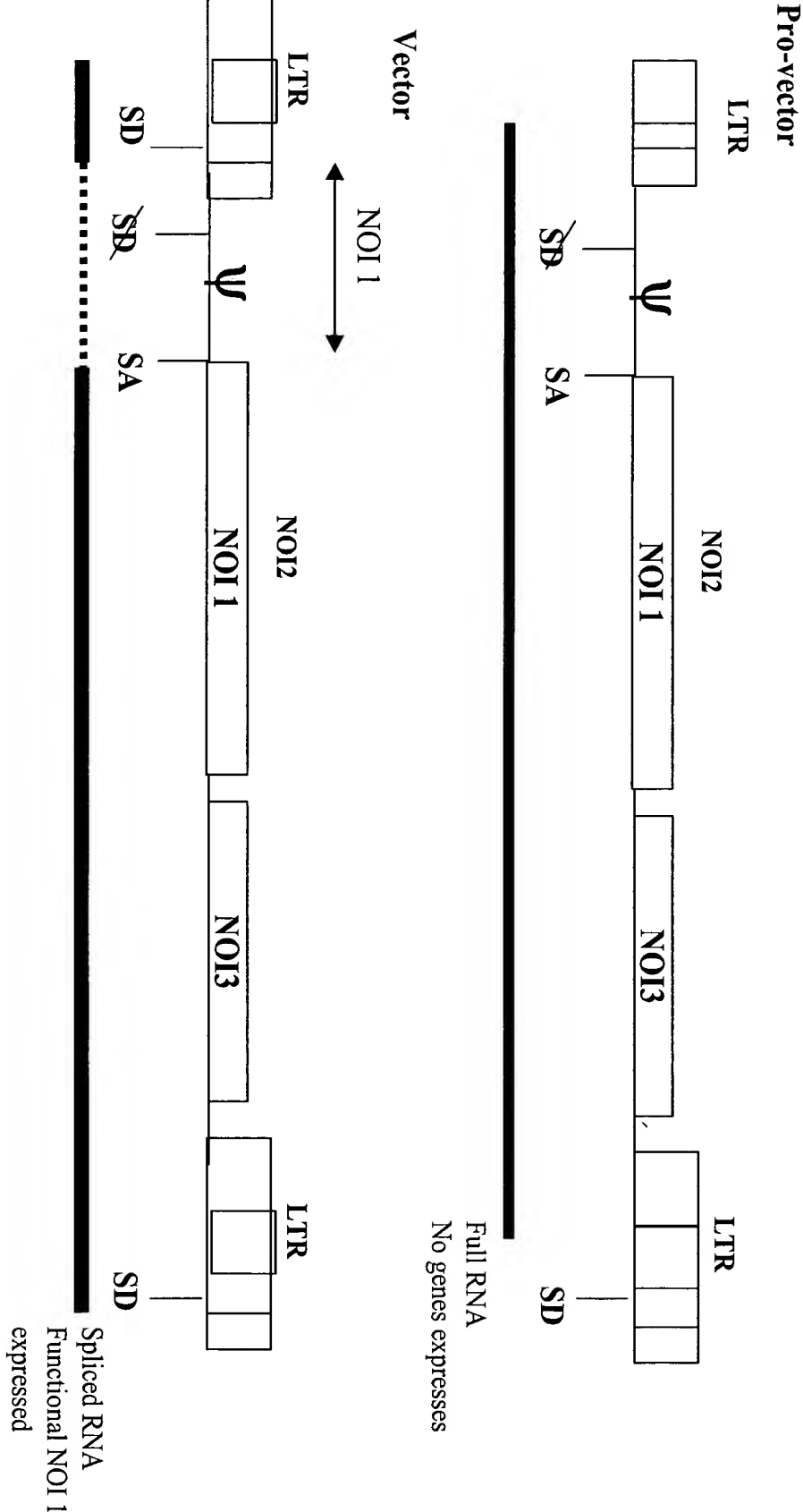


Full RNA  
 genome and  
 selectable marker

Spliced RNA only  
 Expresses NOI 2



Figure 27c cont.



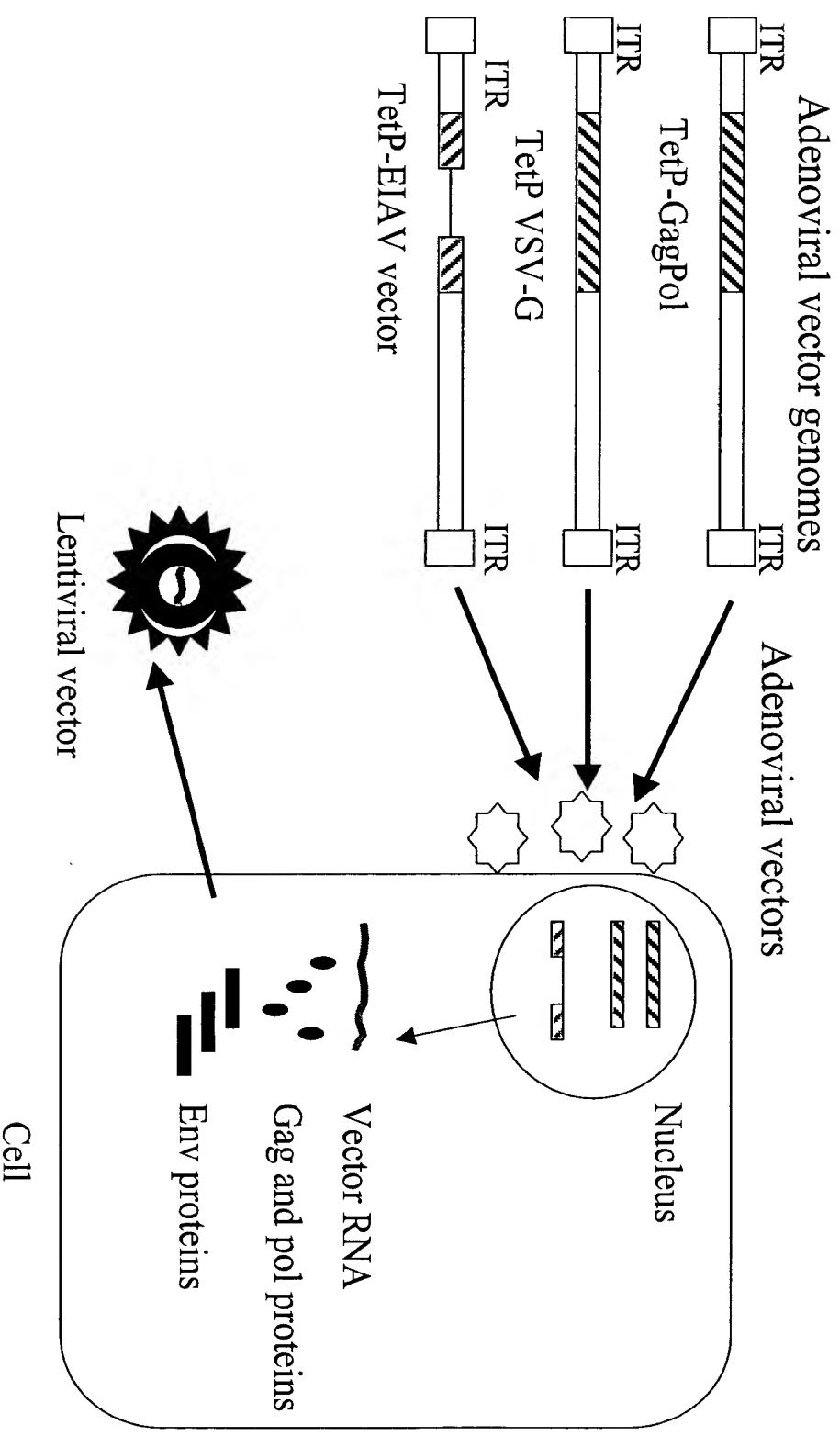


Figure 28

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